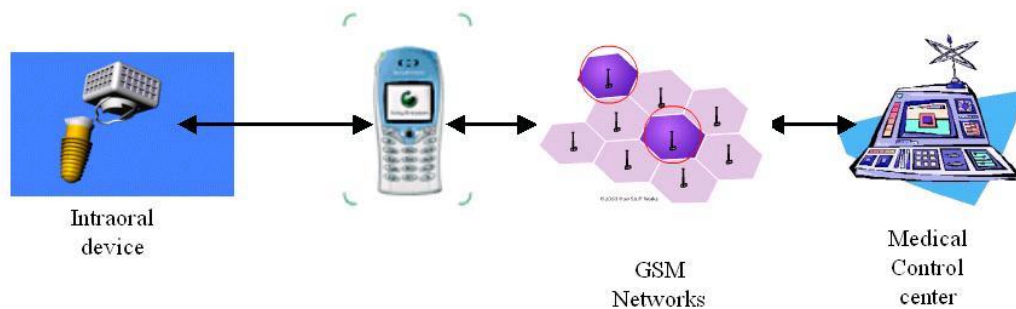


## *Intelligent Intraoral Medicine Delivery Micro-system*

**"DRUGS DON'T WORK IN PATIENTS WHO DON'T TAKE THEM" Everett Koop, M.D.**

This old saying describes one of the major obstacles the \$500 Billion pharma industry is facing. As the R&D expenses for the discovery of new molecules reach new heights of more than \$500 Million per new molecule, the delivery of the drug still depends heavily on patient's behavior and habits. "IntelliDrug" Project, a European Commission FP6 project<sup>1</sup>, comes to address some of those issues by harnessing the new developments in micro-electronics, MEMS and embedded software. The project is aiming at leveraging the unique capabilities of micro electronic and embedded software such as accuracy, flexibility, automation, controllability and communication, while using the latest development in MEMS to interface between the 'microprocessors and software world' and 'molecules and chemical compounds world'. Combining those capabilities together, one gets a device that delivers the selected medicine automatically, on time, in accurate dosing (i.e. tailored to the patient's unique profile such as age, gender, medical status, weight, etc.) and remotely controlled by the patient or by a point of care. Figure 1 depicts the IntelliDrug vision.

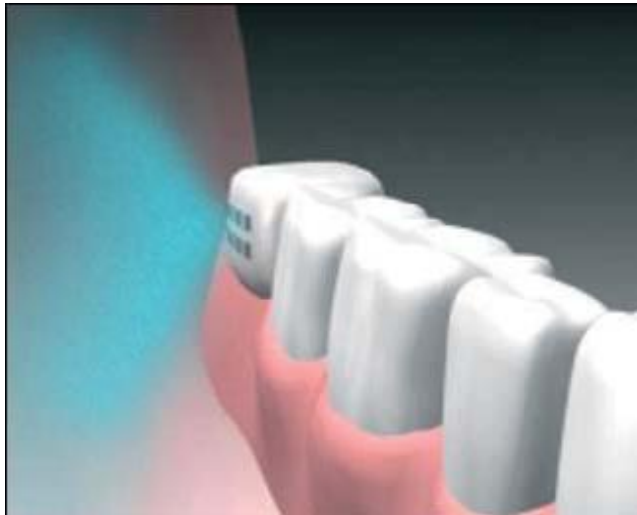


**Figure 1: IntelliDrug vision**

The oral cavity was selected as the preferred location for placing the IntelliDrug device. The main advantages of the oral cavity are: (1) outstanding accessibility, compared to other mucosal surfaces, such as the nasal, rectal, ocular mucosa;

<sup>1</sup> The project is supported by a European grant under the Sixth Framework Programme – IST-FP6 Contract No 002243 and brings together the manpower and technological expertise of 15 partners: HSG-IMIT, Fraunhofer-IBMT, MT–Promedt Consulting, Charité Universitätsmedizin (Germany), Valtronic SA Switzerland), Warsaw University of Technology, ASM Centrum Badań i Analiz Rynku (Poland), Università di Palermo, Università "Federico II" di Napoli (Italy), Hospital Clínico San Carlos, Telefónica (Spain), Assuta Hospital, Relsoft Systems, Bio Dar Ltd. and the Anti Drug Authority (Israel). The overall project management is done by Assuta Medical Centers (Israel). See more at [www.intellidrug.org](http://www.intellidrug.org).

**(2) minimal cosmetic and discretion concerns (compared to the skin and the rectal mucosa, respectively); (3) easy bi-directional transfer of biological substances; (4) high tolerance to trauma due to multiple defense mechanisms (e.g. the presence of saliva and antimicrobial factors and the rapid epithelial regeneration); and (5) rich blood supply, leading to good bioavailability.**



The device that looks like a molar teeth, as shown in an artist concept at Figure 2, releases the drug to the buccal tissue in accordance to the instructions of its built-in microprocessor, which is commanded pre-programmed by embedded software, and on-line by a remote control. Using the built-in clock the drug administration can be automated and scheduled to address chrono-therapy<sup>2</sup> needs.

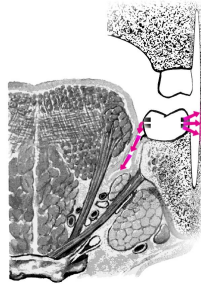
**Figure 2: IntelliDrug device (artist concept)**

Using her/his personal remote control a patient can, as an example, increase or decrease the amount of pain relief drugs administered to his/her body from the IntelliDrug device, matching accurately the momentary needs. In the future, once a distant point of care is connected, and patient's status is transmitted to monitored by it, a doctor at the point of care will be able to control the patient's administered dose, a vital option for elderly patients.

Releasing the drug toward the oral tissues opens a new route for increased medication bioavailability. Many drugs are very poorly absorbed by the body when they are swallowed, as their exposure time in the gastrointestinal tract (GI) before exiting the body is too short. Other drugs do not show a therapeutic effect at all as they are destroyed in the GI or metabolized in the liver. As shown in Figure 3, the drug released from the IntelliDrug device penetrates the body via the oral tissues.

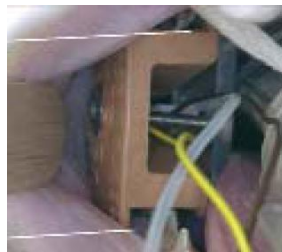
---

<sup>2</sup> Chrono-therapy tries to address the known phenomena, in which the occurrence of certain symptoms is much higher in specific hours of the day. As an example, asthma attacks tend to occur more frequently during the early morning hours, blood pressure tends to rise in the morning, etc.

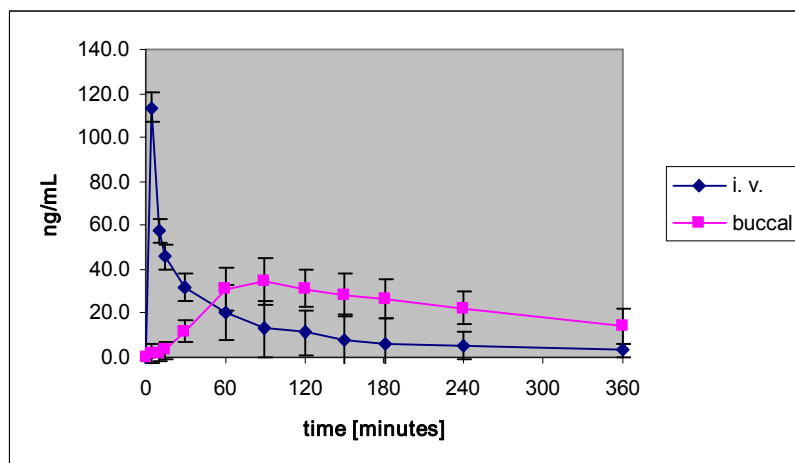


**Figure 3 – IntelliDrug administrating route.** This transversal view of the mouth shows the tooth-like device delivering medication to the cheek (arrows to the right) and to the floor of the mouth (arrows down).

Using a prototype as shown in Figure 4, series of *in vivo* trials were conducted using naltrexone (to treat addiction) and galantamine (to manage Alzheimer’s disease), which were delivered to the buccal mucosa during few minutes. This administration method was compared with intra-venous administration. The blood concentration of those drugs, analysed for up to 30 hours demonstrate an excellent bioavailability using the IntelliDrug method (Figure 5).



**Figure 4 – IntelliDrug prototype used in *in vivo* trials**



**Figure 5 – Intra-venous vs. buccal delivery of naltrexone**